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**UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA**

IN RE: VIAGRA (SILDENAFIL CITRATE)
AND CIALIS (TADALAFIL) PRODUCTS
LIABILITY LITIGATION

Case No. 3:16-md-02691-RS
MDL No. 2691

This Document Relates to:

**DECLARATION OF LOREN H. BROWN
IN SUPPORT OF DEFENDANTS PFIZER
AND LILLY'S MOTION TO EXCLUDE
PLAINTIFFS' EXPERTS' OPINIONS**

ALL ACTIONS

1 I, Loren H. Brown, make this declaration under penalty of perjury in support of
2 Defendants Pfizer Inc. and Eli Lilly and Company's Motion to Exclude Plaintiffs' Experts'
3 Opinions and submit the following information:

4 1. I am an attorney at the law firm DLA Piper LLP (US), counsel of record for
5 Defendant Pfizer Inc. in the above-titled action. I am licensed to practice law in the state of New
6 York and admitted *pro hac vice* in this matter. I make this declaration based on my own personal
7 knowledge and, if called as a witness, could and would testify competently to the matters set forth
8 below.

9 2. I certify that the exhibits included in the attachment hereto are true and correct
10 copies, submitted on behalf of Defendants Pfizer Inc. and Eli Lilly and Company in support of
11 their Motion to Exclude Certain Plaintiffs' Experts' Opinions. True and correct copies of the
12 exhibits listed on the attached are electronically filed with this Court using the CM/ECF system.

13 Dated: January 11, 2019

14 Respectfully submitted,

15 DLA PIPER LLP (US)

16 BY: /s/ Loren H. Brown

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ATTACHMENT

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Exhibit List to Defendants Pfizer and Lilly's Motion to Exclude Plaintiffs' Experts' Opinions

Daubert Defense Ex. #	Description	Date	Orig. Ex. # (If Joint Exhibit has been used as Deposition Exhibit) (if any)
1	Viagra Label	12/14/2017	
2	Cialis Label	2/15/2018	
3	Burnett et al., AUA Educ. & Research, Inc., Erectile Dysfunction: AUA Guideline, Apr. 2018:1-70.	04/2018	
4	Center for Drug Evaluation and Research, VIAGRA Drug Approval Package (Sections 1-10) (Excerpted)	3/27/1998	
5	Pfizer Response to PRAC Request for Supplementary Information, August 29, 2014	8/29/2014	Witte, Ex. 5
6	Sildenafil Toxicopharmacological Expert Report, Appendix 4 (Excerpted)	1/21/2004	
7	Goldstein et al., The Serendipitous Story of Sildenafil: An Unexpected Oral Therapy for Erectile Dysfunction, Sex Med Rev. 2018;1-14.	10/6/2018	
8	FDA Approval Letter for Viagra	3/27/1998	
9	FDA Approval Letter for Cialis	11/21/2003	
10	FDA Supplemental Approval Letter for Cialis	1/7/2008	
11	FDA Supplemental Approval Letter for Cialis	10/6/2011	
12	Lilly Safety Topic Report: Prostate, Bladder, and Skin Cancer	12/2/2014	
13	Lilly Safety Topic Report: Melanoma	12/2/2016	
14	FDA Approval Letter for Revatio	6/3/2005	
15	Revatio Label	2/1/2018	
16	FDA Approval Letter for Adcirca	5/22/2009	
17	Adcirca Label	5/5/2017	
18	US Patent No. 5,858,694 titled Method for Identifying Compounds for Inhibition of Cancerous Lesions	1/12/1999	Piazza Ex. 34
19	Domvri et al., Potential synergistic effect of phosphodiesterase inhibitors with chemotherapy in lung cancer, J Cancer. 2017;8(18):3648-56.	10/9/2017	
20	Booth et al., PDE5 inhibitors enhance the lethality of pemetrexed through inhibition of multiple chaperone proteins and via the actions of cyclic GMP and nitric oxide, Oncotarget. 2017;8(1):1449-68.	1/3/2017	
21	Confino et al., Inhibition of mouse breast adenocarcinoma growth by ablation with intratumoral alpha-irradiation combined with inhibitors of immunosuppression and CpG, Cancer Immunol Immunother. 2016;65(10):1149-58.	10/2016	
22	Tavallai et al., Nexavar/Stivarga and Viagra interact to kill tumor cells, J Cell Physiol. 2015;230(9):2281-98.	9/2015	
23	Black et al., PDE5 inhibitors enhance tumor permeability and efficacy of chemotherapy in a rat brain tumor model, Brain Res. 2008;1230:290-302.	9/16/2008	
24	Sharman et al., Cyclic-GMP-Elevating Agents Suppress Polyposis in ApcMin mice by Targeting the Preneoplastic Epithelium, Cancer Prev Res. 2018;11(2):81-92.	2/2018	
25	Qian et al., Effect of sildenafil citrate on an orthotopic prostate cancer growth and metastasis model, J Urol. 2003;170:994-97.	9/2003	
26	Roberts et al., Curcumin interacts with sildenafil to kill GI tumor cells via endoplasmic reticulum stress and reactive oxygen/ nitrogen species, Oncotarget. 2017;8(59):99451-469.	8/2/2017	
27	Serafini et al., Myeloid-derived suppressor cells promote cross-tolerance in B-cell lymphoma by expanding regulatory T cells, Cancer Res. 2008;68(13):5439-49.	7/1/2008	
28	Greish et al., Sildenafil citrate improves the delivery and anticancer activity of doxorubicin formulations in a mouse model of breast cancer, J Drug Target. 2018;26(7):610-15.	8/2018	
29	Islam et al., Sildenafil Suppresses Inflammation-Driven Colorectal Cancer in Mice, Cancer Prev Res. 2017;10(7):377-388.	7/2017	Piazza Ex. 29
30	Zenitani et al., C-type natriuretic peptide in combination with sildenafil attenuates proliferation of rhabdomyosarcoma cells, Cancer Med. 2016;5(5):795-805.	5/2016	
31	Mei et al., Sildenafil inhibits the growth of human colorectal cancer in vitro and in vivo, Am J Cancer Res. 2015;5(11):3311-24.	10/15/2015	

Exhibit List to Defendants Pfizer and Lilly's Motion to Exclude Plaintiffs' Experts' Opinions

Daubert Defense Ex. #	Description	Date	Orig. Ex. # (If Joint Exhibit has been used as Deposition Exhibit) (if any)
32	Das et al., Sildenafil increases chemotherapeutic efficacy of doxorubicin in prostate cancer and ameliorates cardiac dysfunction, Proc Natl Acad Sci USA. 2010;107(42):18202-07.	10/19/2010	
33	Sponziello et al., PDE5 expression in human thyroid tumors and effects of PDE5 inhibitors on growth and migration of cancer cells, Endocrine. 2015;50(2):434-41.	11/2015	
34	Pendick, Harvard Health Blog	6/5/2014	Piazza Ex. 10
35	Charles Toutant, <i>Lawyers Readying Suits Claiimng Viagra Caused Skin Cancer</i> , N.J. L.J. (LAW.com.)	11/13/2014	
36	Parker, et al. v. Pfizer, Inc. , No. 1522-CC00318 (Mo. Cir. Ct. Feb. 9, 2015)	2/9/2015	
37	Boffetta et al., False-positive results in cancer epidemiology: a plea for epistemological modesty, J Natl Cancer Inst. 2008;100(14):988-995.	7/16/2008	
38	Jiang et al., Socioeconomic and lifestyle factors and melanoma: a systematic review, Br J Dermatol. 2015;172:885-915.	4/2015	
39	Drees et al., 3',5'-Cyclic nucleotide phosphodiesterase in tumor cells as potential target for tumor growth inhibition, Cancer Res. 1993;53:3058-3061.	7/1/1993	Haq Ex. 6; Ganesan Ex. 20
40	Nair and Jacob, A simple practice guide for dose conversion between animals and human, J Basic Clin Pharm. 2016;7(2):27-31.	3/2016	
41	Wang et al., No Causal Link between Phosphodiesterase Type 5 Inhibition and Melanoma, World J Mens Health. 2018;36:e36.	10/10/2018	
42	Pfizer Response to June 03, 2016 FDA Information Request	7/15/2016	
43	Preliminary PRAC Rapporteur Assessment Report on the Signal of Melanoma with Sildenafil	10/13/2014	
44	European Medicines Agency PRAC PSUR Assessment Report Tadalafil	6/11/2015	
45	European Medicines Agency PRAC PSUR Assessment Report Tadalafil	6/9/2017	
46	FDA Division of Epidemiology (DEPI), Review of Published Study Report (FDA00000024)	3/4/2015	
47	FDA Division of Epidemiology (DEPI), Literature Review on the Association Between [PDE5] Inhibitors and Risk of Malignant Melanoma (FDA00000040)	4/27/2016	
48	FDA Division of Pharmacovigilance II, Melanoma and PDE5 Inhibitors (FDA00000001)	8/19/2016	Ballman Ex. 25
49	American Academy of Dermatology, Practice Management Center, <u>Erectile dysfunction drugs and skin cancer</u> .	4/16/2018	Ahmed Ex. 6
50	Weed et al., Tadalafil Reduces Myeloid-Derived Suppressor Cells and Regulatory T Cells and Promotes Tumor Immunity in Patients with Head and Neck Squamous Cell Carcinoma, Clinical Cancer Res. 2015;21(1):39-48.	1/1/2015	Califano Ex. 22
51	Califano et al., Tadalafil Augments Tumor Specific Immunity in Patients with Head and Neck Squamous Cell Carcinoma, Clin Cancer Res. 2015;21(1):30-38.	1/6/2015	Califano Ex. 7; Ballman Ex. 23
52	Pantziarka et al., Repurposing drugs in oncology (ReDo)-selective PDE5 inhibitors as anti-cancer agents, Ecancermedicalscience. 2018;12:824.	4/11/2018	
53	Initial Expert Report of Dr. Singh (<i>In re: Lipitor (Atorvastatin Calcium) Marketing, Sales Practices and Products Liability Litigation</i> , MDL No. 2:14-mn-02502) (Redactions In Original As-Filed Version)	3/4/2015	
54	Supplemental Expert Report of Dr. Singh (<i>In re: Lipitor (Atorvastatin Calcium) Marketing, Sales Practices and Products Liability Litigation</i> , MDL No. 2:14-mn-02502) (Filed Under Seal)	12/7/2015	
55	Turner et al., Thiazolidinediones and associated risk of bladder cancer: a systematic review and meta-analysis, Br J Clin Pharmacol 2013;78:2		
56	Deposition Transcript of Dr. Singh, Vol. 1 and Vol. 2 (Excerpted) (<i>In re: Lipitor (Atorvastatin Calcium) Marketing, Sales Practices and Products Liability Litigation</i> , MDL No. 2:14-mn-02502)	4/28/2015	
57	Dr. Singh Expert Report in <i>Lauris v. Novartis AG</i> , No. 1:16-cv-00393-SHE (E.D. Cal.), Dkt. No. 112-1	6/1/2017	
58	Dr. Singh Expert Report in <i>McWilliams v. Novartis AG</i> , No. 2:17-cv-14302 (S.D. Fla.), Dkt. No. 56-3	2/20/2018	
59	Garrett, et al., Incidence of and Risk Factors for Skin Cancer in Organ Transplant Recipients in the United States, JAMA Dermatol. 2017;153(3):296-303.	3/1/2017	

Exhibit List to Defendants Pfizer and Lilly's Motion to Exclude Plaintiffs' Experts' Opinions

Daubert Defense Ex. #	Description	Date	Orig. Ex. # (If Joint Exhibit has been used as Deposition Exhibit) (if any)
60	Whitt, et al. (Piazza), Sulindac sulfide selectively increases sensitivity of ABCC1 expressing tumor cells to doxorubicin and glutathione depletion, <i>J Biomed Res.</i> 2016;30(2):120-133.	3/2016	Piazza Ex. 18, 40
61	Piazza, Validation of PDE5 as a Chemoprevention Target, <i>Cancer Prev Res.</i> 2017;10(7):373-376.	7/2017	Piazza Ex. 19
62	U.S. Patent Application No. US 20160143912 A1 and U.S. Patent No. 10,039,764 B2 titled Treatment and Diagnosis of Cancer and Precancerous Conditions Using PDE10A Inhibitors and Methods to Measure PDE10A Expression	6/18/2018 (application) 8/7/2018	Piazza Ex. 27
63	US Patent No. 9,365,528 B2 titled Derivatives of Sulindac, Use Thereof and Preparation Thereof	6/14/2016	Piazza Ex. 28
64	El-Sharkawy et al., Design and synthesis of novel annulated thienopyrimidines as phosphodiesterase 5 (PDE5) inhibitors, <i>Arch Pharm.</i> 2018;351(5):e1800018.	5/2018	Piazza Ex. 33
65	US Patent No. 6,156,528 titled Methods for Using a Phosphodiesterase in Pharmaceutical Screening to Identify Compounds for Treatment of Neoplasia	12/5/2000	Piazza Ex. 35
66	Tinsley, et al., Inhibition of PDE5 by sulindac sulfide selectively induces apoptosis and attenuates oncogenic Wnt/β-catenin-mediated transcription in human breast tumor cells., <i>Cancer Prev Res (Phila)</i> 2011;4(8):1275-84.	8/2011	Piazza Ex. 36
67	US Patent No. 9,388,139 B2 titled Derivatives of Celecoxib, Use Thereof and Preparation Thereof	7/12/2016	Piazza Ex. 37
68	Ahmed, et al. (Piazza), Exploring the PDE5 H-pocket by ensemble docking and structure-based design and synthesis of novel β-carboline derivatives, <i>Eur J Med Chem.</i> 2012;57:329-43.	9/24/2012	Piazza Ex. 38
69	Gurpinar et al. (Piazza), COX-independent mechanisms of cancer chemoprevention by anti-inflammatory drugs, <i>Front Oncol.</i> 2013; 3:181.	7/11/2013	Piazza Ex. 39
70	National Cancer Institute, Division of Cancer Prevention, Grant R01CA155638, <i>Phosphodiesterase 5: A Novel Target and Inhibitor for Breast Cancer Chemoprevention</i> , Gary A. Piazza, University of South Alabama	7/6/2018	Piazza Ex. 43
71	Letter from Christine P. Nguyen, FDA Office of Drug Evaluation III, to Pfizer Inc.	6/3/2016	

1 CERTIFICATE OF SERVICE
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6 I hereby certify that a copy of the foregoing was electronically filed through the Court's
7 CM/ECF system on January 11, 2019, which shall send notification of such filing to all CM/ECF
8 participants.
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28 /s/ Loren H. Brown
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